REMARKS

Entry of all amendments before examination of the application is respectfully requested. Claims 1 through 57 are pending in this application. Claims 1, 2, 11, 12, 21, 22, 31, 32 and 33 have been amended. These claims were amended to reference SEQ ID NOS to a sequence listing being filed herewith. The sequences referenced are found in Figures 1 through 6. The Claims 34 through 57 were added in this amendment. Support for these claims is found on page 30, lines 1 through 23. Please enter the Sequence Listing containing SEQ ID NO: 1 through SEQ ID NO: 15. No new matter has been added by these amendments.

In light of the above amendment and remarks, Applicant asserts that the claims are now in condition for allowance. Accordingly, Applicant respectfully requests that the Examiner issue a Letters Patent on the present application.

Applicant authorizes the charging of any required fees to Account No. 06-2375/09807797, from which the undersigned is authorized to draw. If there are any questions regarding this Amendment and Response or the application in general, please do not hesitate to contact the undersigned.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

The paragraph beginning at page 4, line 2 has been amended as follows:

--FIG. 1 shows the 1276 base pair cDNA sequence of gene O1-180 (SEQ ID NO: 1).--

The paragraph beginning at page 4, line 3, has been amended as follows:

--FIG. 2 shows the 361 amino acid sequence that is coded for by gene O1-180 (SEQ ID NO: 2).--

The paragraph beginning at page 4, line 4, has been amended as follows:

--FIG. 3 shows the 1817 base pair cDNA sequence of gene O1-184 (SEQ ID NO: 3).--

The paragraph beginning at page 4, line 5, has been amended as follows:

--FIG. 4 shows the 426 amino acid sequence that is coded for by gene O1-184 (SEQ ID NO: 4).--

The paragraph beginning at page 4, line 6, has been amended as follows:

--FIG. 5 shows the 1019 base pair cDNA sequence of gene O1-236 (SEQ ID NO: 5).--

The paragraph beginning at page 4, line 7, has been amended as follows:

--FIG. 6 shows the 207 amino acid sequence that is coded for by gene O1-236 (SEQ ID NO: 6).--

The paragraph beginning at page 4, line 30, has been amended as follows:

--FIG. 10. Npm2 cDNA representation. Schematic representation of the mouse Npm2 cDNA sequence (984 bp) and two of the clones isolated from the mouse ovary CDNA libraries. The original 01-236 probe (749 bp) is shown at the top and encompasses the entire Npm2 open reading frame. The open reading frame (solid box) is 621 bp and the 5' UTR and 3' UTR

sequences (thin lines) are 155 bp and 205 bp, respectively. The polyA sequences are not depicted. Clone 236-1 was isolated from the wild-type ovary cDNA library and clone 236-3 was isolated from the GDF-9-deficient ovary cDNA library. Clone 236-3 (984 bp excluding polyA sequence) is 4 bp longer at the 5' end and 1 bp longer at the 3' end than clone 236-1 (979 bp excluding polyA sequences). Codon 36 of the open reading frame of both cDNAs is GGC (Glycine; Figure 11) whereas the same codon of the 129SvEv gene is TGC (Cysteine; [Figure 13] Figures 13A and 13B (SEQ ID NO: 7 through SEQ ID NO: 14)).--

The paragraph beginning at page 5, line 28, has been amended as follows:

--FIGS. 13A and 13B. Mouse Npm2 gene (SEQ ID NO: 7 through SEQ ID NO: 14) and amino acid sequences. Uppercase letters represent sequence identity with the Npm2 cDNA sequences; non-transcribed 5' and 3' sequences and intron sequences are shown in lowercase. The predicted transcription initiation codon, the termination codon, and the polyadenylation signal sequence are all underlined. Numbers along the left side represent the amino acids. The underlined and [bloded] bolded "T" in codon 36, the bolded "c" for amino acid 26, and the underlined and bolded "C: in the 3' UTR sequence indicate differences between the cDNA and gene sequences. Arrows indicate where the O1-236 fragment initiates and ends in the cDNA sequence.--

The paragraph beginning at page 10, line 15, has been amended as follows:

--Fragments of proteins are seen to include any peptide that contains 6 contiguous amino acids or more that are identical to 6 contiguous amino acids of either of the sequences shown in Figures 2 (SEQ ID NO: 2), 4 (SEQ ID NO: 4), 6 (SEQ ID NO: 6), 11 and 14. Fragments that contain 7, 8, 9, 10, 11, 12, 13, 14 and 15 or more contiguous amino acids or more that are identical to a corresponding number of amino acids of any of the sequences shown in Figures 2 (SEQ ID NO: 2), 4 (SEQ ID NO: 4), 6 (SEQ ID NO: 6), 11 and 14 are also contemplated. Fragments may be used to generate antibodies. Particularly useful fragments will be those that make up domains of O1-180, O1-184 or O1-236. Domains are defined as portions of the proteins having a discrete tertiary structure and that is maintained in the absence of the remainder of the protein. Such structures can be found by techniques known to those skilled in the art. The protein is partially

digested with a protease such as subtilisin, trypsin, chymotrypsin or the like and then subjected to polyacrylamide gel electrophoresis to separate the protein fragments. The fragments can then be transferred to a PVDF membrane and subjected to micro sequencing to determine the amino acid sequence of the N-terminal of the fragments.--

The paragraph beginning at page 29, line 5, has been amended as follows:

--One of the full length Npm2 cDNAs (clone 236-1) was used to screen a mouse 129SvEv genomic library (Stratagene) to identify the mouse Npm2 gene. 500,000 phage were screened and 12 positive were identified. Two of these overlapping phage clones, 236-13 and 236-14 (~37 kb of total genomic sequence), were used to determine the structure of the mouse Npm2 gene. The mouse Npm2 is encoded by 9 exons and spans ~6.6 kb ([Figures 12 and 13] Figures 12 and 13A and 13B (SEQ ID NO: 7-14)). Two moderate size introns (introns 4 and 5) contribute the majority of the gene size. The initiation ATG codon resides in exon 2 and the termination codon in exon 9. The splice donor and acceptor sites ([Figure 13] Figures 13A and 13B (SEQ ID NO: 7-14)) match well with the consensus sequences found in rodents, and all of the intron-exon boundaries conform to the "GT-AG" rule (Senapathy et al. Methods Enzymol 183:252-278 (1990)). A consensus polyadenylation signal sequence (AATAAA) is found upstream of the polyA tracts which are present in the two isolated cDNAs ([Figure 13] Figures 13A and 13B (SEQ ID NO: 7-14)).--

In the claims:

Claim 1 has been amended as follows:

1. (Amended) Substantially pure O1-180 having the amino acid sequence set forth in Fig. 2 (SEQ ID NO: 2).

Claim 2 has been amended as follows:

2. (Amended) An isolated polynucleotide having the polynucleotide sequence set forth in Fig. 1 (SEQ ID NO: 1).

Claim 11 has been amended as follows:

11. (Amended) Substantially pure O1-184 having the amino acid sequence set forth in Fig. 4 (SEQ ID NO: 4).

Claim 12 has been amended as follows:

12. (Amended) An isolated polynucleotide having the polynucleotide sequence set forth in Fig. 3 (SEQ ID NO: 3).

Please amend claim 21 has been amended as follows:

21. (Amended) Substantially pure O1-236 having the amino acid sequence set forth in Fig. 6 (SEQ ID NO: 6).

Claim 22 has been amended as follows:

22. (Amended) An isolated polynucleotide having the polynucleotide sequence set forth in Fig. 5 (SEQ ID NO: 5).

Claim 31 has been amended as follows:

31. (Amended) An antisense polypeptide encoded by a polynucleotide having a nucleotide sequence complimentary to the polynucleotide sequence set forth in Fig. 1 (SEQ ID NO: 1).

Claim 32 has been amended as follows:

32. (Amended) An antisense polypeptide encoded by a polynucleotide having a nucleotide sequence complimentary to the polynucleotide sequence set forth in Fig. 3 (SEQ ID NO: 3).

Claim 33 has been amended as follows:

33. (Amended) An antisense polypeptide encoded by a polynucleotide having a nucleotide sequence complimentary to the polynucleotide sequence set forth in Fig. 5 (SEQ ID NO: 5).

PENDING CLAIMS AS AMENDED

1. Substantially pure O1-180 having the amino acid sequence set forth in Fig. 2 (SEQ ID NO: 2).

2. An isolated polynucleotide having the polynucleotide sequence set forth in Fig. 1 (SEQ ID NO: 1).

3. The polynucleotide of claim 2, wherein the polynucleotide is isolated from a mammalian cell.

4. The polynucleotide of claim 3, wherein the mammalian cell is selected from the group consisting of mouse, rat, pig, cow and human cell.

5. An expression vector including the polynucleotide of claim 2.

6. The vector of claim 5, wherein the vector is a plasmid.

7. The vector of claim 5, wherein the vector is a viral vector.

8. A host cell containing the vector of claim 5.

9. The host cell of claim 8, wherein the cell is prokaryotic.

10. The host cell of claim 8, wherein the cell is eukaryotic.

11. Substantially pure O1-184 having the amino acid sequence set forth in Fig. 4 (SEQ ID NO: 4).

12. An isolated polynucleotide having the polynucleotide sequence set forth in Fig. 3 (SEQ ID NO: 3)

13. The polynucleotide of claim 12, wherein the polynucleotide is isolated from a mammalian cell.

14. The polynucleotide of claim 13, wherein the mammalian cell is selected from the group consisting of mouse, rat, pig, cow and human cell.

15. An expression vector including the polynucleotide of claim12.

16. The vector of claim 15, wherein the vector is a plasmid.

17. The vector of claim 15, wherein the vector is a viral vector.

18. A host cell containing the vector of claim15.

19. The host cell of claim18, wherein the cell is prokaryotic.

20. The host cell of claim 18, wherein the cell is eukaryotic.

21. Substantially pure O1-236 having the amino acid sequence set forth in Fig. 6 (SEQ ID NO: 6).

22. An isolated polynucleotide having the polynucleotide sequence set forth in Fig. 5 (SEQ ID NO: 5)

23. The polynucleotide of claim 22, wherein the polynucleotide is isolated from a mammalian cell.

24. The polynucleotide of claim 23, wherein the mammalian cell is selected from the group consisting of mouse, rat, pig, cow and human cell.

25. An expression vector including the polynucleotide of claim 22.

26. The vector of claim 25, wherein the vector is a plasmid.

27. The vector of claim 25, wherein the vector is a viral vector.

28. A host cell containing the vector of claim 25.

29. The host cell of claim 28, wherein the cell is prokaryotic.

30. The host cell of claim 28, wherein the cell is eukaryotic.

31. An antisense polypeptide encoded by a polynucleotide having a nucleotide sequence complimentary to the polynucleotide sequence set forth in Fig. 1 (SEQ ID NO: 1).

32. An antisense polypeptide encoded by a polynucleotide having a nucleotide sequence complimentary to the polynucleotide sequence set forth in Fig. 3 (SEQ ID NO: 3).

33. An antisense polypeptide encoded by a polynucleotide having a nucleotide sequence complimentary to the polynucleotide sequence set forth in Fig. 5 (SEQ ID NO: 5).

34. A transgenic mouse comprising a disruption of its genome in the O1-236 (Npm2) gene.

35. The transgenic mouse of claim 34 wherein said disruption is a heterozygous disruption.

36. The transgenic mouse of claim 34 wherein said disruption is a homozygous disruption.

37. The transgenic mouse of claim 34 wherein said disruption alters the fertility of a female transgenic mouse.

38. The method of making a transgenic mouse comprising a disruption of its genome in the O1-236 (Npm2) gene, comprising the steps of:

(a) introducing an O1-236 (Npm2) targeting vector into a mouse embryonic stem cell;

(b) selecting for the mutation of the O1-236 (Npm2) gene in embryonic stem cells;

(c) introducing said mouse embryonic stem cells with the mutation of the O1-236 (Npm2) gene into a mouse blastocyst;

(d) transplanting said mouse blastocyst into a pseudopregnant mouse;

(e) allowing said transplanted mouse blastocyst to develop to term; and

(f) identifying a transgenic mouse comprising a disruption of its genome in the O1-236 (Npm2) gene in at least one allele.

39. The method of claim 38 further comprising the step of breeding two transgenic mice to obtain a transgenic mouse comprising a homozygous disruption of its genome of the O1-236 (Npm2) gene.

40. The method of claim 39 wherein said disruption alters the fertility of a female transgenic mouse.

41. A transgenic mouse comprising a disruption of its genome in the O1-180 gene.

42. The transgenic mouse of claim 41 wherein said disruption is a heterozygous disruption.

43. The transgenic mouse of claim 41 wherein said disruption is a homozygous disruption.

44. The transgenic mouse of claim 41 wherein said disruption alters the fertility of a female transgenic mouse.

45. The method of making a transgenic mouse comprising a disruption of its genome in the O1-180 gene, comprising the steps of:

(a) introducing an O1-180 targeting vector into a mouse embryonic stem cell;

(b) selecting for the mutation of the O1-180 gene in embryonic stem cells;

(c) introducing said mouse embryonic stem cells with the mutation of the O1-180 gene into a mouse blastocyst;

(d) transplanting said mouse blastocyst into a pseudopregnant mouse;

(e) allowing said transplanted mouse blastocyst to develop to term; and

(f) identifying a transgenic mouse comprising a disruption of its genome in the O1-180 gene in at least one allele.

46. The method of claim 45 further comprising the step of breeding two transgenic mice to obtain a transgenic mouse comprising a homozygous disruption of its genome of the O1-180 gene.

47. The method of claim 46 wherein said disruption alters the fertility of a female transgenic mouse.

48. A transgenic mouse comprising a disruption of its genome in the O1-184 gene.

49. The transgenic mouse of claim 48 wherein said disruption is a heterozygous disruption.

50. The transgenic mouse of claim 48 wherein said disruption is a homozygous disruption.

51. The transgenic mouse of claim 48 wherein said disruption alters the fertility of a female transgenic mouse.

52. The method of making a transgenic mouse comprising a disruption of its genome in the O1-184 gene, comprising the steps of:

(a) introducing an O1-184 targeting vector into a mouse embryonic stem cell;

(b) selecting for the mutation of the O1-184 gene in embryonic stem cells;

(c) introducing said mouse embryonic stem cells with the mutation of the O1-184 gene into a mouse blastocyst;

(d) transplanting said mouse blastocyst into a pseudopregnant mouse;

(e) allowing said transplanted mouse blastocyst to develop to term; and

(f) identifying a transgenic mouse comprising a disruption of its genome in the O1-184 gene in at least one allele.

53. The method of claim 52 further comprising the step of breeding two transgenic mice to obtain a transgenic mouse comprising a homozygous disruption of its genome of the O1-184 gene.

54. The method of claim 53 wherein said disruption alters the fertility of a female transgenic mouse.

55. A transgenic mouse comprising a disruption of its genome in more than one of the O1-236 (Npm2), O1-180 or O1-184 genes.

56. The method of making a transgenic mouse comprising a disruption of its genome in more than one of the O1-236 (Npm2), O1-180 or O1-184 genes, comprising the steps of:

(a) introducing more than one of the O1-236 (Npm2), O1-180 or O1-184 targeting vectors into a mouse embryonic stem cell;

(b) selecting for the mutation of the O1-236 (Npm2), O1-180 or O1-184 gene in embryonic stem cells;

(c) introducing said mouse embryonic stem cells with the mutation of the O1-236 (Npm2), O1-180 or O1-184 gene into a mouse blastocyst;

(d) transplanting said mouse blastocyst into a pseudopregnant mouse;

(e) allowing said transplanted mouse blastocyst to develop to term; and

(f) identifying a transgenic mouse comprising a disruption of its genome in more than one of the O1-236 (Npm2), O1-180 or O1-184 genes in at least one allele.

57. The method of claim 56 further comprising the step of breeding two transgenic mice to obtain a transgenic mouse comprising a homozygous disruption of its genome in more than one of the O1-236 (Npm2), O1-180 or O1-184 genes.